Nontechnical Abstract

The purpose of this clinical investigation is to determine if gene therapy can be used to promote the development of new blood vessels in the heart. This should increase blood flow to the heart and consequently reduce chest pain in patients with myocardial ischemia.

Myocardial ischemia is a condition in which there is inadequate blood flow to the heart resulting in chest pain. Often myocardial ischemia is caused by coronary artery disease (CAD). Cardiovascular disease is the number one cause of mortality in the United States, and most cardiovascular deaths are due to CAD. While various medications, angioplasty and/or coronary bypass surgery may be sufficient to relieve chest pain in some patients, these methods are not suitable options for others. Therefore, Vascular Genetics Inc. is investigating the use of gene therapy as a treatment for increasing blood flow to the heart in patients with no other therapeutic options.

The treatment will involve using a standard injection needle to deliver deoxyribonucleic acid (DNA), or genetic material, directly into the beating heart. Once inside the heart muscle, this DNA will direct the muscle cells to make a specific protein called vascular endothelial growth factor 2 (VEGF-2). VEGF-2 is a protein that has been shown to cause the growth of new blood vessels under a variety of conditions. Experiments in the laboratory have suggested that VEGF-2 gene therapy can be used to grow new blood vessels in animals whose arteries have been surgically blocked. Additionally, VEGF-2 gene therapy is being used to increase blood flow and reduce resting leg pain (*i.e.*, ischemic rest pain) in the feet or legs of patients with critical limb ischemia, or leg pain due to decreased blood flow in legs due to blocked arteries.

A similar approach using a closely related gene, the vascular endothelial growth factor-1 (VEGF-1) gene, has already been employed successfully in a small group of patients with exercise-induced chest pain. These clinical gene therapy studies were previously conducted by Jeffrey M. Isner, M.D. VEGF-1 DNA and VEGF-2 DNA have been shown to cause very similar effects in animal experiments. The design of this proposed study is very similar to the design of the previous clinical studies with VEGF-1 DNA.

In summary, Vascular Genetics Inc. is investigating the possibility that the injection of VEGF-2 DNA directly into the oxygen-deprived heart will result in the development of new blood vessels and thereby increase the blood supply to the heart and reduce chest pain.